REMARKS

The present application is directed to methods of detecting anti-tumor autoantibodies in an individual by detecting complexes formed by the binding of autoantibodies in a sample from the individual with tumor marker proteins. **The tumor marker proteins used in the claimed methods are isolated from a bodily fluid obtained from a body cavity or space in which a tumor is or was present in a cancer patient.**

Claims 9-10, 13-14, and 19-38 were previously cancelled. Claims 15-18 were previously withdrawn but are now rejoined for examination. Claims 1-8, 11-12, 15-18, 39-41 and 43-44 are currently under examination. Claims 15 and 16 are amended. No new matter is introduced.

Double Patenting

The Examiner maintained the provisional rejection of Claims 1-8, 11, and 12 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1, 4, and 8 of copending Application No. 10/417,633 ("the '633 application") in view of Robertson *et al.* (WO 99/58978).

As mentioned and discussed previously, applicants respectfully wish to defer the filing of a terminal disclaimer in response to this rejection until allowable subject matter in the '633 application has been established.

The Examiner newly rejected Claims 1-8, 11-12, 15-18 and 39-44 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-22 of US Patent No. 7,402,403. Applicants respectfully wish to defer the filing of a terminal disclaimer in response to this rejection until allowable subject matter in this application has been established.

Rejection under 35 U.S.C. §112, first paragraph

The Examiner asserts that the rejection of Claims 1-8, 11-12, 15-18 and 39-44 under 35 U.S.C. §112, first paragraph, is maintained for lack of enablement. Applicants respectfully traverse the rejection.

The Examiner asserts that the present application does not enable the use of the claimed methods for detecting **any** autoantibody against **any** tumor antigen for **any** cancer, for **any** neoplastic change or early carcinogenic change in asymptomatic patients, for measuring recurrence of cancer or assessing prognosis for a treatment therapy.

Applicants respectfully submit that the claimed method claimed is not a method for detecting **any** autoantibodies, it is a method of detecting **cancer-associated anti-tumor** autoantibodies in a sample from an individual. In addition, the claimed method is not a method for detecting any autoantibody against **any** tumor antigen, it is a method of detecting cancer-associated anti-tumor autoantibodies against **one or more tumor marker proteins prepared from a bodily fluid from a body cavity or space in which a tumor is or was present in one or more cancer patients**. Furthermore, Claims 1 and 2 are not methods for cancer diagnosis. These claims are directed to a method of detecting cancer-associated anti-tumor autoantibodies in the sample from an individual by detecting **complexes** formed by specific binding of the one or more tumor marker proteins prepared from a bodily fluid from a body cavity or space in which a tumor is or was present in one or more cancer patients to cancer-associated anti-tumor autoantibodies in the sample. No correlation with a cancer diagnosis is specifically **required** in these claims.

With respect to the scientifically interesting questions raised by the Examiner, applicants respectfully submit that they previously discovered that individuals **spontaneously** produce cancer-associated anti-tumor autoantibodies to tumor marker antigens *in vivo*. In this application, applicants describe and claim their discovery that tumor marker proteins prepared from a bodily fluid from a body cavity or space in which a tumor is or was present in one or more cancer patients could be successfully used in an assay for the detection of these autoantibodies. Applicants, and most likely others skilled in the art, do not

know the answers to the technical questions posed by the Examiner because these questions require knowledge about the generation of the autoantibodies within the body of the individual, which may vary from one individual to another, and applicants fail to see the relevance of the questions posed by the Examiner to the patentability of the present claims. Applicants' discovery lies in the source and preparation of the tumor marker proteins used to **detect** these spontaneously produced autoantibodies, **not** in the mechanism of action or formation of the autoantibodies themselves.

With regard to Claims 15-18, in the previous Office Action mailed October 30, 2009, the Examiner rejected Claims 1-8, 11, 12 and 39-44 under 35 U.S.C. §112, first paragraph, for lack of enablement. However, Claims 15-18 were **not** rejected. Thus, no rejection of Claims 15-18 under 35 U.S.C. §112, first paragraph, can be **maintained** in the present Office Action because these claims were not previously rejected for lack of enablement. Furthermore, the Examiner admits the claimed method is enabled for MUC1/breast cancer, CA125/ovarian cancer, and MUC1/sarcoma, yet rejects Claims 15 and 16, which specifically name MUC1 and MUC16 (previously known as CA125), for lack of enablement. Clarification is respectfully requested. In any event, applicants submit that **three** working examples in a patent application is **more** than sufficient for a showing of enablement.

For at least the foregoing reasons, applicants respectfully submit that the claims are enabled and request withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Rejection under 35 U.S.C. §102(b)

The Examiner maintained the rejection of Claims 1-8, 11-12 and 39-44 under 35 U.S.C. §102(b) as anticipated by Robertson *et al.* (WO 99/58978, hereinafter "Robertson"). Applicants respectfully traverse.

Applicants respectfully submit that Robertson **fails** to teach the preparation of tumor marker proteins from a bodily fluid from a body cavity or space in which a tumor is or was present in one or more cancer patients as claimed in the present application. The claims of the present application clearly distinguish between the term "bodily fluid **sample"**, which

describes the sample being tested and the "bodily fluid" **source** from which the tumor marker proteins are prepared. When read in context, the Robertson publication also distinguishes between these two terms.

On page 6, lines 1-13 of the Robertson publication, Robertson describe the bodily fluid **sample** that can be tested.

> Because the assay method of the invention [is] performed on a sample of bodily fluids taken from the patient[,] it is essentially non-invasive and can be repeated as often as is thought necessary to build up a profile of the patient's immune response throughout the course of disease. As used herein the term 'bodily fluids' includes plasma, serum, whole blood, urine, sweat, lymph, faeces, cerebrospinal fluid or nipple aspirate. The type of bodily fluid used may vary depending upon the type of cancer involved and the use that the assay is being put to. In general, it is preferred to perform the method on samples of serum or plasma.

When read in full and in context, the term "bodily fluid" referenced in this section of the Robertson publication clearly describes only the bodily fluid **sample** being tested, not the bodily fluid **source** from which the tumor antigens used in the claimed methods are prepared.

Lines 9-22 on page 7 of the Robertson publication teach that the tumor marker antigens used in the panel "may be wild type or mutant tumour marker proteins isolated from samples of **biological fluid** from normal individuals, or from cancer patients or from cell lines expressing the tumour marker protein or they may be full length recombinant tumour marker proteins, viral oncogenic forms of tumour marker proteins or antigenic fragments of any of the aforementioned proteins." (emphasis added) In this section, Robertson is describing biological fluids as a possible source of the antigen. However, this section fails to teach or even suggest the preparation of tumor marker proteins from a bodily fluid **from a body cavity or space in which a tumor is or was present in one or more cancer patients** as claimed in the present application.

Page 8, lines 21-27 of the Robertson publication state, "**As aforementioned**, the assays can be formed using tumour marker antigens which are forms of these proteins isolated from human bodily fluids or from cultured cells or antigenic fragments thereof or

full length or truncated recombinant proteins or antigenic fragments thereof." (emphasis added). This section follows a listing of preferred markers for inclusion into the panel and is merely summarizing the statement made on page 7. No mention is made of the preparation of tumor marker proteins from a bodily fluid **from a body cavity or space in which a tumor is or was present in one or more cancer patients.**

On page 14, line 30, to page 15, line 5 of the Robertson publication, Robertson teaches **serum** from advanced breast cancer patients as a source of MUC1 protein for use in an assay. Robertson compares this MUC1 with MUC1 isolated from **normal** urine and concludes, "MUC1 isolated from the serum of patients with advanced breast cancer is therefore preferred for use as antigen in the panel assay method and the single marker assay methods described herein." Robertson mentions only MUC1 from **normal** urine and never even suggests using urine from a bladder cancer patient as a source of tumor marker antigen.

In light of the foregoing remarks, applicants respectfully submit that Robertson fails to anticipate the claimed method and request withdrawal of the rejection of the claims under 35 U.S.C. §102(b).

Rejection under 35 U.S.C. §112, first paragraph

The Examiner rejected Claims 1-8, 11-12, 15-18 and 39-44 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse the rejection.

The Examiner cites the Written Description Guidelines of January 5, 2001 and concludes that the present specification lacks sufficient characterization of the antigens used in the claimed methods. Applicants respectfully submit that the present application contains working examples, clearly describes the source of antigen as being from a bodily fluid from a body cavity or space in which a tumor is or was present in one or more cancer patients, lists five exemplary bodily fluid useful as sources of the tumor marker protein (ascites, pleural effusion, seroma, hydrocoele and wound drainage fluid), and lists numerous tumor marker

proteins with reference to scientific publications that describe these tumor marker proteins in detail.

For at least the foregoing reasons, applicants respectfully submit that the claims are sufficiently supported by the specification and request withdrawal of the written description rejection under 35 U.S.C. §112, first paragraph.

CONCLUSION

The foregoing is submitted as a full and complete response to the rejections in the Office Action mailed December 8, 2009. No additional fees are believed due, however, the Commissioner is hereby authorized to charge any deficiencies which may be required or credit any overpayment to Deposit Account Number 11-0855.

Applicants assert that the claims are in condition for allowance and respectfully request that the application be passed to issuance. If the Examiner believes that any informalities remain in the case that may be corrected by Examiner's amendment, or that there are any other issues which can be resolved by a telephone interview, a telephone call to the undersigned attorney at (404) 745-2473 is respectfully solicited.

Respectfully submitted,

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